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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/341,119 11/18/99 SAUER

P P63712US0

EXAMINER

HM22/0214

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400 SEVENTH STREET NW
WASHINGTON DC 20004

ART UNIT	PAPER NUMBER
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1651
DATE MAILED:

02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Applicati n No.

09/341,119

Applicant(s)

SAUER ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 November 1999.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

1. The preliminary amendment filed November 18, 1999, has been received and entered.
2. Claims 1-13 are pending and are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph. The specification enables separating plasmid DNA from RNA and linear DNA by preferentially binding plasmid DNA over RNA and linear DNA to a silica support in the presence of a solution comprising 4 M potassium thiocyanate, 0.6 M NaCl, 0.1 M glycine, and 30% ethanol at a pH of 11.25 to 12.0. The specification also enables separating plasmid DNA from RNA and linear DNA by preferentially binding plasmid DNA over RNA and linear DNA to a silica support in the presence of a solution comprising 8.8 M sodium thiocyanate, 0.6 M NaCl, 0.1 M glycine, and 30% ethanol at a pH of 9.2 to 11.1. However, the

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specification does not reasonably provide enablement for using any chaotropic agent at any pH over 8 to separate plasmid DNA from RNA and linear DNA, as currently encompassed by the claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Specifically, although it is an established practice, the art of purifying plasmid DNA by binding the plasmids to silica in the presence of a chaotropic agent is well known to be a highly unpredictable art. For example, Gautsch et al (U.S. Pat. 6,027,750) clearly demonstrate that using certain chaotropic agents at pH 8.0, one cannot even obtain plasmid binding to glass. See Table 2, at cols. 13 and 14. See also, Boom et al, at col. 14, Example A5. Thus, Gautsch and Boom clearly demonstrate that the simple practice of binding plasmid DNA to glass or silica in the presence of a chaotropic agent is in fact a fairly unpredictable art requiring significant experimentation as to the selection and concentration of chaotropic agent, as well as the determination of suitable pH.

The process claimed by applicant adds the additional requirement that the plasmid DNA must preferentially bind to the silica without RNA or linear DNA binding to the silica. As applicant's own examples demonstrate, this also requires

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significant experimentation. See specification at pages 21 and 22. Note specifically that applicant's own examples demonstrate that no binding of either plasmid or linear DNA occurs above pH 12 in the preferred binding solution, despite the fact that such a pH and solution is clearly encompassed by the current claim language. Thus, applicant's own example demonstrates that the claimed objective of preferential plasmid DNA binding cannot be achieved under all of the conditions encompassed by the claims.

Thus, with the exception of the conditions mentioned above, the artisan of ordinary skill clearly would expect to have to undertake a significant amount of experimentation to determine which of the many parameters currently encompassed by the claims is truly suitable for binding plasmid DNA in a manner such that it can be separated from RNA and linear DNA. Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

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5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it recites obtaining circular nucleic acids from a solution containing nucleic acids "other than circular nucleic acids". The claim is confusing as to how one can obtain circular nucleic acids from a mixture which does not contain nucleic acids. Note that changing the recitation "other than" to read -- in addition to -- at line 2 of claim 1 would overcome this ground of rejection.

Regarding claim 2, the phrase "in particular" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claims 3, 5-9, 12 and 13, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

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The recitation "crude" in claim 4 is indefinite because it is not clear what level of purification of bacterial cells is required by the claim. This ground of rejection can be overcome by deleting the term "crude."

The recitation "stucks" in claim 6 is indefinite because it is not clear what applicant means by the recitation. Also, the parenthetical material at the end of claim 6 is indefinite because it is not clear whether the material is intended to be an actual limitation in the claim or merely exemplary of the subject matter it follows.

Claim 8 does not logically follow from claim 1. Claim 1 explicitly recites "a pH > 8" whereas claim 8 recites preparing "a pH of 8 to 12". Since the pH must be greater than 8 according to claim 1, the pH cannot be 8, as recited in claim 8. Also, the recitation "in particular" in claim 8 is indefinite because it is not clear how the recitation is intended to modify the claims.

The recitation "automated manner" in claim 10 is indefinite because it is not clear what actions are required by this recitation and what actions are excluded. The metes and bounds of the claimed subject matter are simply not clear.

The recitation "appropriate conditions" in claim 11 is indefinite because the inquiry into what conditions are

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appropriate is entirely subjective. Thus, two different practitioners might have entirely opposing opinions as to the appropriateness of a single set of identical conditions.

The recitation "preferably" in claim 12 is indefinite because it is not clear when the preference must be exercised.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-6 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (U.S. Pat. 5,075,430) and Marko et al (Anal. Biochem. 121(2):382-387 (1982)).

Each of Little and Marko disclose the preparation of plasmid DNA by binding the plasmid to silica or glass in the presence of a chaotropic agent at pH 8, and in the presence of non-plasmid DNA or RNA species. See, e.g., Little '430 at col. 3, lines 63-68; see also Marko at pages 383-384. Note specifically that Little, at col. 3, lines 44-48, explicitly discloses that in a high concentration of chaotropic agent the silica-containing diatomaceous earth used therein preferentially binds larger DNA over RNA and small DNA linkers. Thus, each of the references differs from the claims only in that the claims recite a pH greater than 8 whereas the prior art uses a pH of 8.

However, keeping in mind the infinitesimally small difference between the claims and the prior art, the artisan of ordinary skill clearly would have had a reasonable expectation that pH values nominally great than 8 would have been useful in binding plasmid DNA to silica supports, based on the prior art's disclosure of the suitability of pH 8 in this type of process. Thus, the artisan of ordinary skill clearly would have been motivated to have used a pH greater than 8 in the processes disclosed by Little and Marko. Moreover, pH is well known to be a result-effective parameter routinely optimized in this type of process. Thus, the determination of a suitable pH range for

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plasmid binding clearly would have been an obvious matter of optimization on the part of the artisan of ordinary skill.

10. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (U.S. Pat. 5,075,430) and Marko et al (Anal. Biochem. 121(2):382-387 (1982) as applied to claims 1-6 and 8-11 above, and in further view of Smith et al (U.S. Pat. 6,027,945) and Segel (*Biochemical Calculations*, pp. 403-406 (Appendix IV), John Wiley & Sons, Inc., New York, 1976).

As discussed above, Little and Marko clearly render obvious Claims 1-6 and 8-11. However, neither of these references discloses the use of magnetic silica particles in the processes disclosed therein. However, Smith clearly discloses the advantageousness of using such particles when purifying DNA by processes using chaotropic reagents. See, e.g., Abstract. Thus, the artisan of ordinary skill at the time of applicant's invention clearly would have been motivated by Smith's disclosure of the advantages of using magnetic silica particles to have used said particles in Little's or Marko's processes. A holding of obviousness over the cited claims is therefore clearly proper.

Lastly, claim 8's substitution of a known buffer such as glycine (see, e.g. Segel at page 406) for the buffer used in

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Little or Marko must clearly be considered a substitution of one known buffer for a known equivalent, and therefore obvious under § 103(a).

11. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bastian et al (WO 95/21849 or U.S. Pat. 6,180,778 B1) in view of Segel (*Biochemical Calculations*, pp. 403-406 (Appendix IV), John Wiley & Sons, Inc., New York, 1976).

Bastian discloses solutions useful in purifying DNA, said solutions comprising chaotropic reagents (which may be thiocyanates), alcohols and buffers. See, e.g. discussion regarding lysis solutions at '778, col. 5, line 54 through col. 6, line 5; see also the various reagents disclosed by '778 at col. 7, line 59 through col. 8, line 18. Thus, the claims differ from the prior art in that the claims use a different chaotropic reagent than used in the prior art and a different buffer. However, the substitution of the known chaotropic agent, sodium thiocyanate, for the thiocyanate reagents in the Bastian references clearly must be considered the substitution of one known thiocyanate chaotropic agent for a known thiocyanate equivalent, and therefore obvious under § 103(a). Similarly, the substitution of a known buffer such as glycine (see, e.g. Segel at page 406) for the buffers used the Bastian

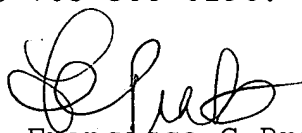
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references must clearly be considered a substitution of one known buffer for a known equivalent, and therefore obvious under § 103(a). Thus, absent a demonstration of something unexpected resulting from the use of these known equivalents, a holding of obviousness is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Francisco C Prats
Primary Examiner
Art Unit 1651

FCP

February 12, 2001